Skyclarys (omaveloxolone) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
10/1/2023	10/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Skyclarys™ (omaveloxolone) Capsule	Treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Friedreich Ataxia	Friedreich ataxia (FA, FRDA) is a progressive autosomal recessive genetic neurodegenerative disorder affecting approximately 5,000 patients in the United States and 22,000 patients globally.(4,5) FA is caused by a biallelic trinucleotide (GAA) repeat expansion in the first intron of the *FXN* gene, which impairs transcription and significantly reduces the amount of functional frataxin protein. The pathological consequences of frataxin deficiency include disruption of iron–sulfur cluster biosynthesis, cellular iron dysregulation, mitochondrial dysfunction, and increased sensitivity to oxidative stress leading to the clinical features of FA.(2,3,4,5) Ataxia is the most common clinical feature in FA, reflecting both proprioceptive loss and cerebellar disease. Patients can also develop spasticity, visual and hearing loss, and non-neurological features such as cardiomyopathy, diabetes, and scoliosis. In most patients, symptoms begin between 5 and 15 years of age, and patients lose the ability to ambulate by their mid-20s. FA shortens life span, most often through consequences of cardiomyopathy; average age at death is 37 years.(4,5) Genetic testing for the triplet repeat expansions in the first intron of the frataxin (*FXN*) gene that cause Friedreich ataxia should be performed in all patients with progressive cerebellar ataxia and autosomal recessive inheritance.(2,3,4,5) Progression in FA is primarily assessed through rating scales, such as the modified Friedreich Ataxia Rating Scale (mFARS). The mFARS is a clinical assessment tool to assess patient function, which consists of 4 domains to evaluate bulbar function, upper limb coordination, lower limb coordination, and upright stability. The mFARS has a maximum score of 99, with a lower score on the mFARS signifying better neurological function (i.e., lesser physical impairment).(1,2,4) Until omaveloxolone was approved by the FDA for treatment of FA, there was no specific disease-modifying therapy available. The management of patients with this disorder requires a multidisciplinary team of special services. An occupational and physical therapy program should be initiated early. Periodic evaluation of cardiac

	function is required. Similarly, patients should be monitored for the development of dysphagia, scoliosis, vision loss, hearing loss, bladder dysfunction, sleep apnea, and diabetes mellitus.(4,5)
Efficacy	Omaveloxolone is an activator of the Nuclear factor-like (Nrf2) pathway, which is involved in the cellular response to oxidative stress.(1) Treatment with omaveloxolone in vitro restores mitochondrial function in fibroblasts from Friedreich ataxia patients and in neurons from multiple mouse models.(4,5) In a larger international randomized trial, 103 patients with Friedreich ataxia (median age, 21 to 22 years; mean disease duration, approximately 4.5 years) were randomly assigned to omaveloxolone 150 mg daily or placebo for 48 weeks. Efficacy data were presented for 82 patients (80%) who received 48 weeks of treatment and had completed primary outcome measurements on the mFARs. Among these patients, mFARS scores improved by 1.55 points in the omaveloxolone group and worsened by 0.85 points in the placebo group (mean difference between groups -2.4 points, 95% CI -4.3 to -0.5). Adverse effects that occurred more commonly with omaveloxolone than placebo included elevated aminotransferase levels (37 versus 2%; no cases of clinical liver injury), headache (37 versus 25%), and nausea (33 versus 14%).(1) Although the trial had limitations and the effect size was relatively modest, Friedreich ataxia is a slowly progressive disease, and small differences in functional progression over one to two years could translate to meaningful differences over the course of the disease.(5)

REFERENCES

Number	Reference
1	Skyclarys prescribing information. Reata Pharmaceuticals, Inc. February 2023.
2	Rummey C, Corben LA, Delatycki M, et al. Natural History of Friedreich Ataxia. Neurology. 2022 Oct;99(14):e1499-e1510.
3	Pandolfo M. Friedreich Ataxia. Arch Neurol. 2008 Oct;65(10):1296-1303.
4	Lynch DR, Chin MP, Delatycki MB, et al. Safety and Efficacy of Omaveloxolone in Friedreich Ataxia (MOXIe Study). Ann Neurol. 2021 Feb;89(2):212-225.
5	Opal P, Zoghbi H, et al. Friedreich Ataxia. UpToDate. Last updated January 2023. Literature review current through February 2023.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Skyclarys	omaveloxolone cap	50 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Skyclarys	omaveloxolone cap	50 MG	90	Capsules	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Skyclarys	omaveloxolone cap	50 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Skyclarys	omaveloxolone cap	50 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** Skyclarys

Module	Clinical Criteria for Approval
	1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of Friedreich ataxia (FA, FRDA) with genetic analysis confirming mutation in the frataxin (FXN) gene **AND** 2. The prescriber has assessed the patient's baseline (prior to therapy with the requested agent) neurological function (as scored by the modified Friedreich Ataxia Rating Scale [mFARS]) **AND** 3. If the patient has an FDA approved indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, geneticist, neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval**: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had improvements or stabilization with the requested agent (e.g., improvement in mFARS score) **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, geneticist, neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval**: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND**

Module	Clinical Criteria for Approval
	C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval:** 12 months